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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,664	02/03/2006	Gisela G Chiang	13751-036US1/A167 US	7404

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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
09/07/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/519,664	CHIANG ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-11,14-16,18,20 and 25-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-11, 14-16, 18, 20, and 25-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 7/14/10 in response to the Office Action of 1/15/10 are acknowledged and have been entered.

Claims 1, 6-11, 14-16, 18, 20, and 25-38 are pending and are currently under examination.

Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6-11, 14-16, 18 and 20-38 remain rejected under 35 U.S.C. 102(e) as being anticipated by US 20030219871 A1 (the effective filing date of April 02, 2002 to US 60369307) for the reasons stated in the Office Action of 1/15/10 and for the reasons set-forth below.

US 20030219871 A1 teaches a stable hamster host cell lines that can be grown in suspension in serum free medium comprising an increased amount of human Bcl-X_L protein produced by a plasmid expression vector that has been introduced to the cells, wherein the cells comprise a second plasmid expression vector encoding a polypeptide,

that is a secreted protein (see [0095]-[0096] and claim 3, in particular). US 20030219871 A1 further teaches that the level of intracellular anti-apoptotic acting genes (such as Bcl-X_L protein) can substantially improve cell viability without showing any negative effect on cell productivity (see [0014], in particular). US 20030219871 A1 further teaches wherein said second expression vector encodes a light and/or heavy chains of an antibody (see [0098], in particular). US 20030219871 A1 further teaches a method of producing polypeptide of said second expression vector and isolating said polypeptide from the medium of cell culture (see [0096], in particular). US 20030219871 A1 does not teach said cell line must express a heterologous cyclin-dependent kinase inhibitor. Further, such cells are adapted to grow in butyrate.

In the Reply of 7/14/10, Applicant argues that the Office Action of 1/15/10 contains no remarks explaining which portions of the reference anticipate the claims. Applicant further argues that US 20030219871 A1 does not teach CHO cells comprising an increased amount of Bcl-X_L.

The arguments found in the Reply of 7/14/10 have been carefully considered, but are not deemed persuasive. In regards to the argument that the Office Action of 1/15/10 contains no remarks explaining which portions of the reference anticipate the claims, the Office Action of 1/15/10 clearly cited the portions of the reference which anticipate the claims. In a different manner, citation of portions of the reference which anticipate the claims is done above.

In regards to the argument that that US 20030219871 A1 does not teach CHO cells comprising an increased amount of Bcl-X_L, US 20030219871 A1 teaches hamster

cell lines containing increased amounts of Bcl-X_L (see [0095], in particular) and that such hamster cell lines include CHO (see claim 3, in particular).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6-11, 14-16, 18 and 20-38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kim and Lee (IDS filed on 10/22/2007, Biotechnology and Bioengineering, vol. 71, 2000/2001) in view of Mastrangelo (2000, IDS filed on 10/22/2007, Biotechnology and Bioengineering, vol. 67, pages 544-554) for the reasons stated in the Office Action of 1/15/10 and for the reasons set-forth below.

The different between the Cho cells taught by Kim and Lee (IDS filed on 10/22/2007, Biotechnology and Bioengineering, vol. 71, 2000/2001) and the instantly claimed invention is that the Cho cells taught by Kim and Lee is stably transfected with Bcl-2, not Bcl-XL.

Mastrangelo et al teaches that the over expression of bcl-2 family members enhances survival of mammalian cells in response to various culture conditions. The cited art specifically teaches genetically engineered BHK-bcl-xL and CHO-bcl-xL cells which were cloned under selection pressure (paragraph flanking pages 545-546, in particular). The cited art further teaches production of recombinant protein of interest

(CAT and IL-12) in the genetically engineered CHO and BJK cell lines that express anti-apoptotic bcl-xL gene (page 546 col.2 para. 3, page 547, col.1 para.2, page 549, fig-5, page 550, fig-8, page 551, fig-11, page 552, fig-12). The cited art further teaches that cellular life spans were doubled in both BHK-bcl2 and CHO-bclx(L) cells relative to the parental cell lines. Furthermore, the presence of these gene products provided increases of up to 2-fold in recombinant CAT production. Similarly, overexpression of bcl-2 and bcl-x(L) genes also increases IL-12 production in the CHO and BHK cells. The cited art clearly establishes that the overexpression of bcl-2 family member genes can have a significant impact on culture viabilities and recombinant protein production in mammalian cells (see page 544, abstract).

Thus it would have been obvious to one ordinary skilled in the art at the time the instant invention was made to modify Kim and Lee by substituting Bcl-XL taught by Mastrangelo et al., instead of Bcl-2. One would have been motivated to do so since Mastrangelo et al., teaches that "even during such harsh treatment, Bcl-XL was able to enhance the survival of both cultures, providing CHO cells with viable numbers that were nearly 20-fold that of the controls after five days of exposure". Note abstract of Mastrangelo et al.

In the Reply of 7/14/10, Applicant argues that Kim does not disclose a stable cell line that overexpresses Bcl-2 and produces an increased amount of a recombinant secreted protein. In regards to the discrepancies in the pages identified in the introductory paragraph and text passages cited in the rejection found in the Office Action of 1/15/10, it is noted that the pages identified in the introductory paragraph have

been clarified above. Applicant further argues that expressing Bcl-XL in CHO cells provides the unexpected result of producing more protein production per cell without the application of butyrate (see Figure 13 of the instant specification). Applicant further states that this unexpected result makes Bcl-XL expression advantageous over other apoptosis inhibitors such as Bcl-2 and that Bcl-XL and Bcl-2 are not functional equivalents because expressing Bcl-2 in CHO cells has not been shown to result in producing more protein production per cell without the application of butyrate.

The arguments found in the Reply of 7/14/10 have been carefully considered, but are not deemed persuasive. In regards to the argument that that Kim does not disclose a stable cell line that overexpresses Bcl-2 and produces an increased amount of a recombinant secreted protein, Kim teaches a stable cell line that overexpresses Bcl-2 (see page 185, in particular) and produces an increased amount of a recombinant secreted protein (see "thereby increasing antibody production" at right column on page 190, in particular).

In regards to the argument that expressing Bcl-X_L in CHO cells provides the unexpected result of producing more protein production per cell without the application of butyrate (see Figure 13 of the instant specification), production of increased protein by expressing an anti-apoptotic protein such as Bcl-X_L is expected due to increased cell survival. Further, the instant claims encompass (and particularly claim) methods wherein cells are cultured in butyrate (see instant claims 8 and 27, in particular).

In regards to the argument that Bcl-XL and Bcl-2 are not functional equivalents because expressing Bcl-2 in CHO cells has not been shown to result in producing more

protein production per cell without the application of butyrate, the examiner agrees that expressing Bcl-2 in CHO cells has not been shown to result in producing more protein production per cell without the application of butyrate. Such a lack of showing supports that producing more protein per cell by expressing Bcl-XL in CHO cells is not unexpected because one would not know what to expect on a per cell basis.

Summary

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on 571-272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Primary Examiner, Art Unit 1642